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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,080	02/27/2001	Mark J. O'Connor	117-328	5965

7590 01/15/2003

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EXAMINER
SALIMI, ALI REZA

ART UNIT	PAPER NUMBER
1648	18

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/701,080	Applicant(s) O'Connor et al
	Examiner A. R. SALMI	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *11/12/02; 9/19/02* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *36, 40-43, 45, 46, and 53-57* is/are pending in the application.

4a) Of the above, claim(s) *45 and 46* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *36, 40-43, and 53-57* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *8*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

This is a response to the amendment C, paper No.6, filed 9/20/2002. Claims 37-39, 44, 47-52 have been canceled. Claims 56-57 have been added. Claims 36, 40-43, 45, 46, 53-57 are pending.

Election/Restriction

Applicant's election with traverse of Group I (claims 36-43, 53-57) in Paper No. 6 is acknowledged. The traversal is on the ground(s) that Groups I and II as amended are linked by a special technical feature and form a ingle general inventive concept. This is not found persuasive because they are drawn to patentably distinct methods, group I is directed to determining whether a compound is capable of inhibiting two polypeptide complex. In contrast, the method of claim 45 is directed to a method of identifying a compound that interacts with a particular polypeptide. 37 CFR 1.475(b) does not provide for multiple independent methods.

The requirement is still deemed proper and is therefore made FINAL.

Claims 45, and 46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

Applicants are reminded to cancel the claims to the non elected claims.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

Claims 36-43, 53-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 is vague and indefinite for recitation of "disrupting" or "disrupts", the term "disrupting" or "disrupts" is a relative term. The term "disrupting" or "disrupts" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition, the claim is indefinite for recitation of "comprises" this is an open language and the intended metes and bounds of the "first polypeptide comprises a TRAM" is not defined. Moreover, the claim is objected to for recitation of "TRAM", the entire name should be present followed by its acronym. It's not clear whether TRAM is a trademark or a generic name. In addition, the claim is indefinite for polypeptide "comprising a TRIM sequence", "comprising" is open language and the intended metes and bounds of the "comprising" has not be defined, the intended "TRIM" sequence is not defined. Furthermore, claim is objected to for recitation of

" show in in" in line 13, is "shown in" intended? Still further, the intended papillomavirus is not defined, is L1 of HPV intended? Also, the claim is confusing for recitation of "(b) determining", yet no steps are present as to how this determination is formed and/or observed. This affects the dependent claims.

Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the specific sequence of "TRAM" should be provided, right now the SEQ ID NO: 1 is a general formula, a specific sequence for "TRIM" should be provided, the determining step should be defined, how is the determining made?

Claim 43 is vague and indefinite for recitation of "mdm2, CBP, and p300", what are these? The intended polypeptide(s) should be identified by a specific sequence number. In addition, please spell out full names, followed by their acronyms.

Claim 53 is vague and indefinite for recitation of "CBP", what does this mean? The intended polypeptide should be identified by a specific sequence number. In addition, please spell out "CBPs" full name.

Claims 54 and 55 are rejected to because they depend from canceled claim 52. To purse with compact prosecution "claims 54, and 55 have been treated as claims depending from independent claim 36. However, this does not relieve the applicant from addressing the problem with the said claims in future correspondence.

In addition, Claim 54 is vague and indefinite, the intended TRIM sequence within the second zinc finger is not defined, the intended sequences should be identified by a specific sequence identification

number (s).

Claim 57 is confusing for recitation of "amino acids 1B to 147", what is "1B"? Is "100 to 147" intended?

Claim Rejections - 35 USC § 112

Claims 36-43, 53-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method of identifying compounds that inhibit the interaction of transcriptional adaptor motif (TRAM) wherein the TRAM sequences are any of the sequences identified as SEQ ID Nos: 3-9 with human papillomavirus (HPV) E6 protein of either HPV-16 or HPV-18, does not reasonably provide enablement for a method of determining a compound capable of inhibiting or "disrupting" any and all of TRAM polypeptide as the first protein interacting with any and all HPV proteins as second protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected,

to make or use the invention commensurate in scope with these claims. At the onset Applicants are reminded that this field is highly unpredictable and its the disclosure that should provide adequate teaching for one of ordinary skill in the art to enable the claimed invention absent undue experimentations. The disclosure of the Applicants in itself is evidence for unpredictability of the field, and the state of the art. First, the specification does not provide any teaching wherein the method can be practiced in a multi cellular organism (animal), hence, the limitation of in vitro should be present. Cell culture is known as an in vitro to all ordinary skill in the art and the Office accepts what is routinely understood amongst the practitioners. The specification has no *in vivo* study and the limitation of in vitro should be present so one of skill in the art would be appraised of the scope of the invention. Second, the specification asserts that only the E6 proteins of human papilloma viruses from so called "high risk" (groups that are known to cause cervical cancer) where able to be utilized in the method wherein the E6 protein showed the ability to bind specific TRAM sequences (for instance see the specification on page 47), and as further evidence see the post filing publication by Zimmermann et al, Journal of Virology, Aug. 1999, Vol. 73, No. 8, pp. 6209-6219, see the abstract, which clearly indicates the E6 of HPVs that are known to cause cervical cancer have the capacity to bound specific TRAM proteins only (emphasis added). However, the scope of the claimed invention is not reflective of state of the art and it would be undue experimentation for one of ordinary skill in the art to determine which protein of HPV in general and which HPV E6 protein in particular to utilize in the method.

Third, the current method is non-enabling within the scope of claimed invention, since there are so many variables present which would not allow one of ordinary skill in the art to enable the claimed methods absent undue experimentation. For example, the SEQ ID NO: 1 in its present form is a general formula, and in order for one of ordinary skill in the art to enable the claimed invention one has to figure out first which TRAM protein should be present, then which TRIM should be present that is capable of binding the TRAM. Then the actual testing of a particular compound that is capable of inhibiting the binding would have to be conducted. In reality this method has three variables and three unknowns. Applicants' method should specifically define two of the variables so the third variable can be determined. It is very important to have specific TRAM protein and specific TRIM protein where one of ordinary skill in the art would know for certain the actual binding would take place. Hence, skilled artisan can look for the compounds that would inhibit the said binding. Applicants should not ask others to determine which TRAM and TRIM are needed. To provide a general formula such as SEQ ID NO: 1 would lead to innumerable combinations and sub-combinations of TRAM that should be determine to see whether or not it can be utilized as a TRAM, since not all TRAM are able to bind to even E6 (see page 45 of the specification) wherein only CBP II domain proteins are capable of binding HPV-16 E6, specifically proteins SEQ ID NO: 3 to 9. In addition, if papillomavirus protein is not defined, hence, one has to determine which part of the large virus should be utilized. The claims in their current form would provide either large number of false positive and/or large number of false negative results which would be undue experimentation. A large number of compounds would be

regarded as non-inhibitory where in reality if both specific TRAM and TRIMs are defined would perhaps be categorize as capable of inhibitory, and vis versa. Therefore, with regard to an unpredictable field, this does not constitute an adequate disclosure. See Fiers v. Revel (25USPQ2d 1601 at 1606; and also decision by the Federal Circuit with regard to the enablement issues see Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1001-1007). For example, the CAFC stated that "It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement." (See page 1005 of the decision). This means that the disclosure must adequately guide the art worker to determine, without undue experimentation. The applicant can not rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-43, 53-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are broadly drawn to multitude of TRAM molecules. In contrast, the specification only describes sequences consisting of a sequence identified as SEQ ID NO: 3 to 9, and its method of use to interact with E6 protein of either HPV-16 or HPV-18. Applicants do not describe other molecules encompassed by the claims, and the structural features that distinguish all such proteins from other proteins that are not provided and the method of their use. If applicants were not in possession of the sequences that fall within the limitation that are now present then they were not is possession of the method of using either. In order, to practice the method of claim 36 one should be in possession of the specific sequence. Providing a general formula is not indicative of possession.

Hence, Applicants have not, in fact, described the molecules that are within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed general sequence, it is not clear the Applicant was in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 36-43, 53-57 are rejected under 35 U.S.C. 102(e) as being anticipated by Androphy et al (U.S 5,821,051).

The teaching and the claims of the above cited world patent clearly anticipates the broad limitations of the claimed method. The above cited patent taught a method of testing the effects of compounds on the E6-binding proteins (see for example the claims 2-14).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36-43, 53-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Chene et al (WO 97/11367).

The teaching and the claims of the above cited world patent clearly anticipates the broad limitations of the claimed method. The above cited patent taught a method of testing the effect of compounds on the binding of dm2 and p53 (see the claims). The proteins cited in the above cited patent meets the broad limitation of TRIM of applicants claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 36-43, 53-57 are rejected under 35 U.S.C. 102(a) as being anticipated by Lane et al (WO 98/01467).

The teaching and the claims of the above cited world patent clearly anticipates the broad limitations of the claimed method. The above cited patent taught a method of

testing the effect of compounds on the binding of MDM2 and p53 (see the claims, and abstract). The peptides disclosed meet the broad limitations of TRAM.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salami whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James House, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salami

1/14/2003

ALI R. SALIMI
PRIMARY EXAMINER